Identification of a specific reprogramming-associated epigenetic signature in human induced pluripotent stem cells.

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Public Summary:
In this study, we demonstrated that there are consistent differences in both the chemical modifications and the activities of the genome between human embryonic stem cells and human induced pluripotent stem cells.

Scientific Abstract:
Generation of human induced pluripotent stem cells (hiPSCs) by the expression of specific transcription factors depends on successful epigenetic reprogramming to a pluripotent state. Although hiPSCs and human embryonic stem cells (hESCs) display a similar epigenome, recent reports demonstrated the persistence of specific epigenetic marks from the somatic cell type of origin and aberrant methylation patterns in hiPSCs. However, it remains unknown whether the use of different somatic cell sources, encompassing variable levels of selection pressure during reprogramming, influences the level of epigenetic aberrations in hiPSCs. In this work, we characterized the epigenomic integrity of 17 hiPSC lines derived from six different cell types with varied reprogramming efficiencies. We demonstrate that epigenetic aberrations are a general feature of the hiPSC state and are independent of the somatic cell source. Interestingly, we observe that the reprogramming efficiency of somatic cell lines inversely correlates with the amount of methylation change needed to acquire pluripotency. Additionally, we determine that both shared and line-specific epigenetic aberrations in hiPSCs can directly translate into changes in gene expression in both the pluripotent and differentiated states. Significantly, our analysis of different hiPSC lines from multiple cell types of origin allow us to identify a reprogramming-specific epigenetic signature comprised of nine aberrantly methylated genes that is able to segregate hESC and hiPSC lines regardless of the somatic cell source or differentiation state.

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